

REMARKS

THE AMENDMENTS

Applicant has withdrawn Claim 4 and amended claims 8-10 and 14 to reflect applicant's election in response to the Restriction Requirement. Claim 8 has been further amended as discussed below to improve its form. Claim 2 has been amended to correct its form. Applicant has canceled claims 5 and 18 without prejudice. Upon entry of the amendments, claims 2-3, 8-10, 14, and 19 will be pending in the present application.

Applicants have further amended claim 10 to recited that the marker "...is a tumor suppressor gene disease marker." Support for this amendment is found throughout the specification, e.g., at page 1, lines 4-13; page 2, lines 15 to 34; page 4, lines 13-20; and page 4 line 30 to page 7, line 15.

These amendments are made without prejudice and without waiver of applicants' right to pursue any canceled subject matter in one or more applications claiming priority herefrom under 35 U.S.C. § 120.

These amendments add no new matter.

Applicants request reconsideration of the above-identified application, in view of the above amendments and the following remarks.

REJECTIONS

35 U.S.C. §112, Second Paragraph

Claims 5, 8 and 18 are rejected under 35 U.S.C. § 112, second paragraph, as "indefinite." Office Action, page 3.

Applicant's cancellation of claims 5 and 18, renders moot the rejection of these claims.

The Examiner asserts that claim 8 lacks antecedent basis. Applicants have amended claim 8 to reflect the proper antecedent basis in claim 19 from which it depends.

Claim 8 complies with 35 U.S.C. § 112, second paragraph. Accordingly, applicants request the Examiner withdraw this rejection.

35 U.S.C. §103(a)

Claims 2, 3, 5, 8, 9, 14, and 19 stand rejected under 35 U.S.C. 103(a) as "unpatentable" over Allione et al. ("Allione") in view of United States patent 5,945,522 ("Cohen") and United States patent 5,624,819 ("Skolnick").

The Examiner contends that it would have been obvious to one of ordinary skill in the art at the time of filing of the instant application to combine the teaching of Allione with Cohen and Skolnick to arrive at the method of the present application. Applicant traverses.

The claims of the instant application are directed to a method for determining if an offspring of an individual afflicted with a tumor suppressor gene disease has an increased risk of developing the tumor suppressor gene disease. The method of the invention comprises establishing the loss of an allele (Loss of Heterozygosity) in the tumor of an afflicted individual and, based on the amplification of one or more polymorphous DNA microsatellite markers in the blood of an offspring of the afflicted individual, determining whether the lost allele or the retained allele of the afflicted individual was inherited by the offspring. In this method, the presence in the offspring of the allele that is retained in the tumor of the afflicted individual indicates an increased risk of developing the tumor suppressor gene disease. According to the method of the invention, the retained microsatellite marker(s) are a means for "tagging" the disease-causing allele.

Allione refers to the determination of loss of heterozygosity in patients with breast carcinomas.

Allione, however, is silent about the importance of the determination of *which* allele is retained in the tumor.

Rather, Allione, thus, merely refers to detecting loss of heterozygosity. Loss of heterozygosity is insufficient to determine whether an offspring of an afflicted individual is at risk for developing diseases. In contrast, in the claimed invention, it is the presence in the offspring of the allele that is retained in the tumor of the afflicted individual that indicates an increased risk of developing the tumor suppressor gene disease. Therefore, the present invention goes one step beyond determining loss of heterozygosity; the present invention identifies the allele that is retained in the tumor of the afflicted individual (and looks for that particular allele in the blood of the offspring).

Nothing in Allione, thus, teaches or suggests determining which allele of the afflicted parent was inherited. Neither Cohen nor Skolnick cure the deficiencies of Allione. Neither of those documents makes any mention of determining *which* allele of the afflicted parent was inherited. None of the cited documents either

alone or in any combination teach or suggest the claimed invention. The cited documents, thus, cannot render obvious the claimed invention. Applicant requests reconsideration and withdrawal of this rejection.

Claims 2, 3, 5, 8-10, 14, 18 and 19 stand rejected under 35 U.S.C. 103(a) as "unpatentable" over United States patent 5,945,522 ("Cohen") in view of United States patent 5,624,819 ("Skolnick") and Jacoby et al. ("Jacoby").

The Examiner contends that it would have been obvious to one of ordinary skill in the art at the time of filing of the instant application to combine the teaching of Cohen with Jacoby and Skolnick to arrive at the method of the present application. Applicant traverses.

Cohen refers to the mapping technique of loss of heterozygosity, but contains no teaching of the steps of the claimed invention. Specifically, Cohen does not teach amplification of one or more polymorphous DNA microsatellite markers from the tumor and blood of an afflicted individual, comparison of the amount and length of these markers and establishing a loss of allele based on the comparison, and further looking at microsatellite markers in the blood of an offspring to determine which

allele was inherited. Skolnick does not cure these deficiencies of Cohen.

Jacoby does not cure the deficiencies of Cohen.
No presymptomatic or prenatal diagnosis was carried out in Jacoby. Rather, the purpose of NF2 mutation analysis and linkage analysis using NF2 markers in Jacoby was to examine the pathogenesis and mechanism of schwannomatosis. Jacoby was silent to predicting risk of offspring.

As outlined above, Cohen neither teaches nor suggests the steps of the claimed invention. Neither Skolnick nor Jacoby cure the deficiencies of Cohen. Neither of those documents teach the steps of the claimed invention. None of the cited documents either alone or in any combination teach or suggest the claimed invention. The cited documents, thus, cannot render obvious the claimed invention. Applicant requests reconsideration and withdrawal of this rejection.

Provisional Obviousness-Type Double Patenting

Claims 2, 3, 5, 8-10, 14, 18, and 19 stand provisionally rejected for nonstatutory obviousness-type double patenting as "unpatentable" over claims 1-16 of U.S.

Application No. 10/692,537
Amendment and Reply dated January 16, 2007
Reply to Office Action of August 15, 2006


Patent No. 6,660,477, for reasons detailed in the August
15, 2006 Office Action.

Applicants stand ready to file a Terminal
Disclaimer upon the Examiner's indication of allowable
subject matter in this application.

CONCLUSION

In view of the foregoing amendments and remarks,
applicants respectfully request that the Examiner withdraw
all the objections and rejections and allow all of the
claims of this application.

Respectfully submitted,

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